REMARKS

Reconsideration is respectfully requested.

Claims 1-17, 19 and 20 are under examination. Claims 1-17, 19 and 20 stand rejected. Claim 18 has been withdrawn from consideration and claims 21-22 were previously canceled as being drawn to a non-elected invention. Claims 10 and 15-20 are currently canceled. Claims 1-5, 8, and 11-13 are currently amended. New claims 23-40 have been added. With these amendments, claims 1-9, 11-14 and 23-40 are pending.

Applicants have not dedicated or abandoned unclaimed subject matter, and have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Amendments to Claims

Claims 15-20 are canceled solely to expedite prosecution of the application. Applicants reserve the right to file one or more continuation applications directed to the canceled subject matter.

Claims 1 and 2 are amended by deleting the terms "or prevention" and "or preventing."

Claims 1 and 2 are also amended by replacing "a prodrug of a GABA analog" with "1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid".. Claim 11 is also amended to clarify that "prodrug" means "1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof". Support for these amendments can be found, for example on page 45, lines 12-13 together with Formula (V), page 43, line 27 through page 44, line 2 of the specification as originally filed.

Claim 3 is amended to recite that the GABA analog prodrug is "crystalline 1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid." New claim 23 also specifies that the GABA analog prodrug is "crystalline 1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid." Support for the

amendment to claim 3 and for new claim 23 can be found, for example, at page 45, lines 3-8 of the specification as originally filed.

Claim 4 and new claim 24 recite that "the patient is an adult and the 1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid or a pharmaceutically acceptable salt, hydrate or solvate thereof is administered in a dose of 300 to 3600 mg gabapentin equivalents per day." Support for this amendment can be found, for example, at page 60, lines 23-26 of the specification as originally filed.

The dependencies of claims 4, 5, 8, and 11 are amended to make explicit that which was implicit in the claims as originally filed. Claim 9 is amended to maintain proper claim dependency. Support for claim 9 may be found in claim 8 of the application as filed.

Claim 12 is amended to recite that the "pharmaceutical composition" of claim 2 is a sustained release oral dosage form. Support for this amendment can be found, for example, at page 50, lines 32-34, of the specification as originally filed and page 52, line 1 to page 29, line 22. In view of this amendment, claim 12 is amended to depend only from claim 2, which provides antecedent basis for the claim element "pharmaceutical composition."

In view of the amendment to claim 2, which recites the gabapentin prodrug, 1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid, claim 13 is amended to recite the corresponding GABA analog, 1-(aminomethyl)cyclohexane acetic acid, i.e., gabapentin.

New claims 25 and 26 recite 1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid, and new claim 27 recites that the patient is an adult and the 1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid can be administered in a dose of 300 to 3600 mg gabapentin equivalents per day. Support for these claims can be found, for example, at page 45, lines 12-13, and at page 60, lines 23-26, of the specification.

New claim 28 specifies that the patient is menopausal. Support for this amendment can be found, for example, from page 5, line 14 and page 47, line 24 of the application as originally filed.

New claims 29 to 34 further characterize crystalline 1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid. Crystalline 1-{[(α-

isobutanoyloxyethoxy)carbonyl]-aminomethyl}-1-cyclohexane acetic acid is disclosed in Estrada *et al.*, (US2005/0154057), which is incorporated by reference in its entirety (see page 45, lines 3-8 and page 65, lines 12-23 of the application as originally filed).

Support for new claims 29 to 31 can be found, for example, from Example 3 and Figure 1 of Estrada *et al.* (US 2005/0154057).

Support for new claim 32 can be found, for example, from claim 2 of Estrada *et al.* (US 2005/0154057) in combination with Example 3 and Figure 1.

Support for new claim 33 can be found, for example, in Example 4 of Estrada *et al.* (US 2005/0154057).

Support for new claim 34 can be found, for example, in Example 5 of Estrada *et al.* (US 2005/0154057).

New claims 35, 36, and 40 are supported by page 5, lines 13 to 15 and page 47, lines 21 to 25.

New claim 37 is amended to depend from claim 8 and to recite that the hot-flashes are drug-induced. Support for this amendment can be found, for example, in original claim 9 and at page 47, lines 28-32, of the specification.

Support for new claims 38 and 39 can be found, for example, paragraph [0039] of Estrada *et al.* (US 2005/0154057).

Thus, the amendments to the claims are fully supported by the specification as originally filed and add no new matter.

Claim Rejections – 35 U.S.C. § 112, first paragraph (enablement)

Previous claims 1-17, 19, and 20 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement (Office Action, pages 2-6). The basis of the rejection is that the specification does not reasonably provide enablement for preventing hot flashes with a prodrug of a GABA analog.

Solely to advance prosecution, Applicants have amended independent claims 1 and 2 to delete the phrases "or preventing" and "or prevention". Pending claims 3-9, 11-14, and 23-40

depend from and therefore incorporate each of the elements of amended independent claims 1 and 2. In view of the amendments made to claims 1 and 2, the Examiner's rejection is now moot.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection of previous claims 1-17, 19, and 20 as failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph.

Claim Rejections – 35 U.S.C. § 103(a) (Office Action pages 7-8)

Previous claims 1-17, 19, and 20 stand rejected under 35 U.S.C. § 103(a) as being obvious over Guttuso, Jr., US 6,310,098 B1, in view of R&D Focus Drug News, December 9, 2002. Applicants respectfully traverse.

A claimed invention is unpatentable if the differences between it and the cited references "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a). "For a chemical compound, a *prima facie* case of obviousness requires 'structural similarity between claimed and prior art subject matter . . . where the prior art gives reason or motivation to make the claimed compositions.'" *Yamanouchi Pharmaceutical Co., Ltd. V. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000), quoting *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir 1990) (en banc).

The Examiner alleges that "Guttuso, Jr. teaches [a] method of treating hot flashes comprising administering gabapentin in a male or female." The Examiner further alleges that "R&D Focus Drug News teaches Gabapentin XP (also known as gabapentin enacarbil) is a prodrug of gabapentin" and that "gabapentin enacarbil demonstrated dose-proportional blood levels of active gabapentin, following oral administration and it is better absorbed into the colon than gabapentin itself." The Examiner concludes that "it would have been obvious to one of ordinary skill in the art to employ Gabapentin XP for the treatment of hot flashes in men or women", and that "one would have been motivated to make such a modification in order to achieve expected benefit of "prodrug"of gabapentin". The Examiner states that there is "a reasonable expectation of success . . . because Gabapentin is known in the art by Guttuso, Jr. for

having effectiveness in treating hot flashes and because Gabapentin XP is a prodrug of Gabapentin [that] converts to Gabapentin in vivo as taught by R&D Focus Drug News."

Obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. *MPEP* § 2141.02 V, p. 2100-125, Rev. 6, Sept. 2007, citing *In re Rijckaert*, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993). In the present case, the report in R&D Focus Drug News dated December 9, 2002 did not disclose the chemical structure of Gabapentin XP. Instead, the Report discloses that "Gabapentin XP, a prodrug of gabapentin, is undergoing preclinical evaluation with XenoPort." The text of the report does not disclose the chemical structure of "Gabapentin XP" or associate the "Gabapentin XP" compound with any chemical name or other identifier that would enable one skilled in the art to determine the chemical structure of the compound.

While the STN Database indexing the report as accessed in 2008 does associate "Gabapentin XP" with XP13512 and gabapentin enacarbil, this information was not publicly available in December 2002, and only appears in the database as indexed at the time it was accessed by the Examiner. As of March 31, 2003, the earliest priority date of the instant application, "Gabapentin XP" had not been associated with the chemical name "gabapentin enacarbil." Therefore, as of March 31, 2003, one skilled in the art could not know the chemical structure of "Gabapentin XP" based on the R&D Focus Drug News report either alone or in combination with publicly disclosed information. Certainly, absent knowledge of the chemical structure of "Gabapentin XP," one skilled in the chemical arts cannot apply the requisite factual inquiries for an obviousness analysis as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) of "determining the scope and contents of the prior art" and "ascertaining the differences between the prior art and the claims at issue," e.g., comparing Gabapentin XP with 1-{[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid. The alleged obviousness of the rejected claims cannot be predicated the R&D Focus Drug News, which never published the chemical structure of {[(α-isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid before the filing date of the instant application.

Because the text of the R&D Focus Drug News report cited by the Examiner as prior art does not provide chemical structural detail required to make 1-{[(α-

isobutanoyloxyethoxy)carbonyl]aminomethyl}-1-cyclohexane acetic acid, either alone or in combination with publicly available knowledge, the Examiner has failed to establish a *prima facie* case of obviousness for amended independent claims 1 and 2 as well as claims 3-9, 11-14 and 23-40 which depend therefrom (*MPEP* § 2141.02 V, p. 2100-125, Rev. 6, Sept. 2007; *MPEP* § 2143.03, p. 2100-142, Rev. 6, Sept. 2007; citing *In re Fine* 837 F.2d 1071 (Fed. Cir. 1988)).

In view of the foregoing, Applicants request the withdrawal of the rejection of previous claims 1-17, 19, and 20 as obvious under 35 U.S.C. § 103(a) over Guttuso in view of R&D Focus Drug News.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that the claims satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, and are not obvious under 35 U.S.C. § 103(a) over the cited references. Applicants therefore respectfully request the Examiner's reconsideration of the application and the timely allowance of the claims.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-352-1117.

Respectfully submitted,
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